Application No.: 10/848,741

Kesponse to Utnee Action dated November 19, 2004

Filed: May 20, 2004 Docket No.:

Page 2 of 21

#### IN THE CLAIMS:

This listing of claims replaces all prior versions, and listings, of claims in the application.

#### Listing of the Claims

### 1. (Currently Amended) A compound of the formula

$$(W^4)_q$$
 $(Y^1)_a$ 
 $(Y^3)_c$ 
 $(W^2)_n$ 
 $(W^2)_n$ 
 $(W^2)_n$ 

wherein:

Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup>, and Y<sup>4</sup>, are independently on the ortho, meta or para position on the phenyl rings, and are independently hydrogen, alkyl, cycloalkyl, aryl, alkylaryl, arylalkyl, heteroaryl, or an alkyl, cycloalkyl, aryl, alkylaryl, arylalkyl, or heteroaryl group substituted with 1 to 4 hydrophilic groups selected from hydroxy, alkoxy, -C(O)OR<sup>5</sup>, -SOR<sup>6</sup>, -SO<sub>2</sub>R<sup>6</sup>, nitro, amido, ureido, carbamato, -SR<sup>7</sup>, -NR<sup>8</sup>R<sup>9</sup>, or polyalkyleneoxide; or a substituent represented by the following formula:

$$-X$$
— $(CR^1R^2)_{\bar{i}}$ — $Z$  (2)

provided that at least one four of Y1, Y2, Y3, and Y4 represents formula (2);

X is oxygen or sulfur;

BEST AVAILABLE COPY

Applicants: Harrao Wu, et al. Application No.: 10/848,741

Filed: May 20, 2004

Docket No.: Page 3 of 21 Response to Utilice Action dated November 19, 2004

R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup> are independently selected from hydrogen and C<sub>1</sub> to C<sub>4</sub> alkyi;

Z is a carborane cluster comprising at least two carbon atoms and at least three boron atoms, or at least one carbon atom and at least five boron atoms, within a cage structure;

r is 0 or an integer from 1 to 20;

W1, W2, W3, and W4 are hydrophilic groups independently selected from hydroxy, alkoxy, -C(O)OR5, -SOR6, -SO2R6, nitro, amido, ureido, carbamato, -SR7, -NR8R9, or polyalkylene oxide;

a, b, c, and d independently represent an integer from 1 to 4;

m, n, p, and q are independently 0 or an integer from 1 to 4;

provided that at least one of m, n, p, and q is not zero, and each of the sums a + m, b + n, c + p, and d + q, independently represents an integer from 1 to 5; and

M is either two hydrogen ions; a single monovalent metal ion; two monovalent metal ions; a divalent metal ion; a trivalent metal ion; a tetravalent metal ion; a pentavalent metal ion; a hexavalent metal ion; a radioactive metal ion useful in radioisotopemediated radiation therapy or imageable by single photon emission computed tomography (SPECT) or positron emission tomography (PET); a paramagnetic metal ion detectable by magnetic resonance imaging (MRI); a metal ion suitable for boron neutron capture therapy (BNCT) or photodynamic therapy (PDT); or a combination thereof; wherein the porphyrin metal complex derived from when M is a single monovalent metal ion, a porphyrin-metal complex is produced which is chargebalanced by a counter cation, ; and the perphyrin-metal complex derived from when M is a trivalent, tetravalent, pentavalent, or hexavalent metal ion, a porphyrin-metal complex is produced which is charge-balanced by an appropriate number of counter anions, dianions, or trianions.

Response to Uffice Action dated November 19, 2004

Applicants: Haitao Wu, et al. Application No.: 10/848,741

Filed: May 20, 2004

Docket No.: Page 4 of 21

- 2. (Original) The compound according to claim 1 wherein Z is selected from the carboranes -C2HB9H10 or -C2HB10H10, wherein -C2HB9H10 is nido ortho-, meta-, or para-carborane, and -C2HB10H10 is closo ortho-, meta-, or para-carborane.
- 3. (Original) The compound according to claim 1, wherein M is vanadium, manganese, iron, ruthenium, technetium, chromium, platinum, cobalt, nickel, copper, zinc, germanium, indium, tin, yttrium, gold, barium, tungsten, or gadolinium.
- 4. (Currently Amended) The compound according to claim 1 wherein a b, c, and d are 1, and  $Y^1$ ,  $Y^2$ ,  $Y^3$ , and  $Y^4$  are represented by  $X^4$  $-X-(CR^1R^2)-Z$ <del>(2)</del>
- 5. (Original) The compound according to claim 4 wherein Z is selected from the carboranes -C2HB9H10 or -C2HB10 H10, wherein -C2HB9H10 is nido ortho-, meta-, or para-carborane, and -C<sub>2</sub>HB<sub>10</sub>H<sub>10</sub> is closo ortho-, meta-, or para-carborane.
- 6. (Original) The compound according to claim 5, wherein M is vanadium, manganese, iron, ruthenium, technetium, chromium, platinum, cobalt, nickel, copper, zinc, germanium, indium, tin, yttrium, gold, barium, tungsten, or gadolinium.
- 7. (Original) The compound according to claim 6, wherein X is O; R<sup>1</sup> and  $R^2$  are H; r is 1; and m, n, p and q are each 1.
- (Original) The compound according to claim 7 wherein Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup>, and 8. Y<sup>4</sup> are in the para position on the phenyl ring, and W<sup>1</sup>, W<sup>2</sup>, W<sup>3</sup>, and W<sup>4</sup> are independently, hydroxy or alkoxy groups.
- 9. (Original) The compound according to claim 8 wherein W<sup>1</sup>, W<sup>2</sup>, W<sup>3</sup> and W4 are alkoxy groups.
- 10. (Original) The compound according to claim 9 wherein the alkoxy groups are methoxy groups.

Application No.: 10/848,741

Filed: May 20, 2004

Docket No.: Page 5 of 21

Response to Utilice Action dated November 19, 2004

- 11. (Original) The compound according to claim 10 wherein the methoxy groups are in the meta position of the phenyl ring.
- 12. (Original) The compound according to claim 8 wherein  $W^1$ ,  $W^2$ ,  $W^3$ , and  $W^4$  are hydroxy groups.
- 13. (Original) The compound according to claim 10 wherein the hydroxy groups are in the meta position of the phenyl ring.
- 14. (Currently Amended) The A method of imaging a tumor and surrounding tissue in a subject comprising the administration to the subject of a composition comprising a compound according to claim 1; and the imaging of said subject by a method selected from magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), or positron emission tomography (PET) methods.
- 15. (Currently Amended) A method of imaging a tumor and surrounding tissue in a subject comprising the administration to the subject of a composition comprising a compound according to claim 11; and the imaging of said subject by a method selected from magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), or positron emission tomography (PET) methods.
- 16. (Currently Amended) A method of imaging a tumor and surrounding tissue in a subject comprising the administration to the subject of a composition comprising a compound according to claim 13; and the imaging of said subject by a method selected from magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), or positron emission tomography (PET) methods.
- 17. (Cancelled)
- 18. (Original) A method of bimodal cancer treatment in a subject comprising the administration to the subject of a composition comprising a compound according to claim 1; and the irradiation of said subject.

Response to Ullice Action dated November 19, 2004

Applicants: Hartao Wu, et al. Application No.: 10/848,741

Filed: May 20, 2004 Docket No.:

Page 6 of 21

- 19. (Original) A method of bimodal cancer treatment in a subject comprising the administration to the subject of a composition comprising a compound according to claim 11; and the irradiation of said subject.
- 20. (Original) A method of bimodal cancer treatment in a subject comprising the administration to the subject of a composition comprising a compound according to claim 13; and the irradiation of said subject.
- 21. (Original) The method according to any of claims 18, 19, or 20 wherein said irradiation is by a method utilizing thermal or epithermal neutrons, or laser red light.
- 22. (Original) The method according to any of claims 18, 19, or 20 wherein said bimodal cancer treatment comprises boron neutron capture therapy (BNCT).
- 23. (Original) The method according to any of claims 18, 19, or 20 wherein said bimodal cancer treatment comprises photodynamic therapy (PDT).
- 24. (Original) The method according to any of claims 18, 19, or 20 wherein said bimodal cancer treatment utilizes single photon emission computed tomography (SPECT) or positron emission tomography (PET) wherein M is a SPECT- and/or PET-imageable radioactive metal ion.
- 25. (Original) The method according to any of claims 18, 19, or 20 wherein said bimodal cancer treatment utilizes magnetic resonance imaging (MRI) wherein M is a paramagnetic metal ion.

26-27. (Cancelled)

Applicants: Haitao Wu, et al. Application No.: 10/848,741

Filed: May 20, 2004

Docket No.: Page 7 of 21

### Response to Office Action dated November 19, 2004

#### 28. (New) A compound of the formula

$$(W^4)_q$$
 $(Y^4)_d$ 
 $(Y^1)_a$ 
 $(Y^3)_c$ 
 $(W^2)_n$ 
 $(W^2)_n$ 
 $(Y^2)_b$ 
 $(Y^2)_b$ 
 $(Y^2)_b$ 
 $(Y^2)_b$ 

wherein:

Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup>, and Y<sup>4</sup>, are independently on the ortho, meta or para position on the phenyl rings, and are independently hydrogen, alkyl, cycloalkyl, aryl, alkylaryl, arylalkyl, heteroaryl, or an alkyl, cycloalkyl, aryl, alkylaryl, arylalkyl, or heteroaryl group substituted with 1 to 4 hydrophilic groups selected from hydroxy, alkoxy, -C(O)OR<sup>5</sup>, -SOR<sup>6</sup>, -SO<sub>2</sub>R<sup>6</sup>, nitro, amido, ureido, carbamato, -SR<sup>7</sup>, -NR<sup>8</sup>R<sup>9</sup>, or polyalkyleneoxide; or a substituent represented by the following formula:

$$-X$$
---(CR<sup>1</sup>R<sup>2</sup>)<sub>r</sub>---Z (2)

provided that at least four of Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup>, and Y<sup>4</sup> represents formula (2);

X is oxygen or sulfur;

 $R^1$ ,  $R^2$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ , and  $R^9$  are independently selected from hydrogen and  $C_1$  to  $C_4$  alkyl;

Z is a carborane cluster comprising at least two carbon atoms and at least three boron

Response to Office Action dated November 19, 2004

Applicants: Haitao wu, et al. Application No.: 10/848,741

Filed: May 20, 2004

Docket No.: Page 8 of 21

atoms, or at least one carbon atom and at least five boron atoms, within a cage structure;

r is 0 or an integer from 1 to 20;

W1, W2, W3, and W4 are hydrophilic groups independently selected from hydroxy, alkoxy, -C(0)OR5, -SOR6, -SO2R6, nitro, amido, ureido, carbamato, -SR7, -NR8R9, or polyalkylene oxide;

a, b, c, and d independently represent an integer from 1 to 4;

m, n, p, and q are independently 0 or an integer from 1 to 4;

provided that at least one of m, n, p, and q is not zero, and each of the sums a + m, b + n, c + p, and d + q, independently represents an integer from 1 to 5; and

M is a trivalent, tetravalent, pentavalent, or hexavalent metal ion, thereby producing a porphyrin-metal complex; and

wherein the porphyrin-metal complex is charge-balanced by one or more porphyrin compounds containing a divalent negative charge.

29. (New) The compound according to claim 28 wherein said one or more porphyrin compounds containing a divalent negative charge are represented by the formula

Applicants: Hamao wu, et al. Application No.: 10/848,741

Kesponse to Ultice Action dated November 19, 2004

Filed: May 20, 2004 Docket No.:

Page 9 of 21

JAN. 31. 2005

$$(W^4)_q$$
  $(W^1)_m$   $(Y^1)_a$   $(W^3)_c$   $(W^2)_n$ 

wherein:

 $Y^1$ ,  $Y^2$ ,  $Y^3$ , and  $Y^4$ , are independently on the ortho, meta or para position on the phenyl rings, and are independently hydrogen, alkyl, cycloalkyl, aryl, alkylaryl, arylalkyl, heteroaryl, or an alkyl, cycloalkyl, aryl, alkylaryl, arylalkyl, or heteroaryl group substituted with 1 to 4 hydrophilic groups selected from hydroxy, alkoxy, -  $C(O)OR^5$ ,  $-SOR^6$ ,  $-SO_2R^6$ , nitro, amido, ureido, carbamato,  $-SR^7$ ,  $-NR^8R^9$ , or polyalkyleneoxide; or a substituent represented by the following formula:

$$-X - (CR^1R^2)_{\bar{i}} - Z$$
 (2)

provided that at least four of Y1, Y2, Y3, and Y4 represents formula (2);

X is oxygen or sulfur;

R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup> are independently selected from hydrogen and C<sub>1</sub> to C<sub>4</sub> alkyl;

Z is a carborane cluster comprising at least two carbon atoms and at least three boron atoms, or at least one carbon atom and at least five boron atoms, within a cage structure;

Response to Ultice Action dated November 19, 2004

Applicants: Haitao Wu, et al. Application No.: 10/848,741

Filed: May 20, 2004

Docket No.: Page 10 of 21

r is 0 or an integer from 1 to 20;

W<sup>1</sup>, W<sup>2</sup>, W<sup>3</sup>, and W<sup>4</sup> are hydrophilic groups independently selected from hydroxy, alkoxy, -C(O)OR<sup>5</sup>, -SOR<sup>6</sup>, -SO<sub>2</sub>R<sup>6</sup>, nitro, amido, ureido, carbamato, -SR<sup>7</sup>, -NR<sup>8</sup>R<sup>9</sup>, or polyalkylene oxide;

a, b, c, and d independently represent an integer from 1 to 4;

m, n, p, and q are independently 0 or an integer from 1 to 4; and

provided that at least one of m, n, p, and q is not zero, and each of the sums a + m, b + n, c + p, and d + q, independently represents an integer from 1 to 5.

# This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:
☐ BLACK BORDERS
☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
☐ FADED TEXT OR DRAWING
☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
☐ SKEWED/SLANTED IMAGES
☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
☐ GRAY SCALE DOCUMENTS
LINES OR MARKS ON ORIGINAL DOCUMENT
☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

# IMAGES ARE BEST AVAILABLE COPY.

OTHER:

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.